



09/02/04

1615/1FW

RESPONSE TO OFFICE ACTION MAILED BY USPTO 2 June 04

TO: Commissioner for Patents
P.O. BOX 1450
Alexandria, VA 22313-1450

ATTENTION: Robert M. Joynes, Patent Examiner

APPLICATION No. 09/835, 501

FROM: Tyler Parr
P.O. BOX 371
Chula Vista, CA 91912

Argument made by Patent Reviewer :

1. not synergy, but L-ornithine alone responsible for observed rise in measured 1.5 hour growth hormone levels
2. Prior patent by Giampapa (US 5895625) already patented this technique.

RESPONSE TO #1

Normal (untreated) growth hormone release occurs in first 3 hours of sleep. High levels of supplemental L-ornithine increase total night time growth hormone release, but does so in a manner that disrupts this normal process by initially causing a disruption of the normal sleep cycle patterns

due to the massive polyamine stimulating properties of high levels of supplemental L-ornithine . L-ornithine is the direct precursor to the cellular stimulating polyamines. Thus, while the effects of high levels of supplemental L-ornithine are to substantially increase the total night time growth hormone release levels, they do so in a manner that disrupts sleep cycle timing and thus abrogates the normal 1.5 hour firsts sleep cycle release for which this is avoided by the method described in this patent application. The profoundly altered timing and physiological properties of high supplemental ornithine triggered night time growth hormone release is so disturbing to the normal process, that high level supplementation with L-ornithine for this purpose is expressly recommended against in medical text books due to this disruption of normal sleep cycle events (1).

The purpose of measuring and reporting the 1.5 hour (normal physiological period) growth hormone release by supplemental L-ornithine (alone) at the 500 milligram level was to demonstrate that up this limit, there is no augmentation of the 1.5 hour normal physiological release of growth hormone, but there will certainly be high total night time growth hormone released by such large supplements of L-ornithine. These higher level of growth hormone release with large levels of ornithine occurring later in the night than the 1.5 hour measured period.. This 1.5 hour after sleep was chosen as it is the normal physiological period for 'NORMAL' growth hormone release. Later period of growth hormone release by high levels of supplemental l-ornithine represents a potentially dangerous alteration of

normal physiology of growth hormone release that has been recommended against in the medical literature as cited above (1). This is a physiological problem with high levels of L-ornithine supplementation. It simply alters normal physiological rhythms of night time growth hormone release in a profound way that is strongly recommended against by the medical literature.

It is also possible to augment release of night time growth hormone release by taking large quantities of certain bioflavonoids at sleep that similarly profoundly disturb the normal process and lead to huge growth hormone release levels that create a growth hormone caused tissue swelling that invariably generates a profound 2-3 day headache. This is another example of a profoundly unphysiological augmentation that dysregulates a process, one that would never be chosen due to its profound physiological consequences. The use of high levels of supplemental night time L-ornithine also dysregulates a normal process, producing profoundly impaired normal biological rhythms of growth hormone release that shift release to later in the night and disturb important physiological events like the first few sleep cycles. Using high supplemental doses of night time L-ornithine has as little biological good sense as taking injections of supplemental (exogenous) growth hormone, which also profoundly dysregulates normal production by feedback inhibition of one's own growth hormone production. Augmenting normal biological processes rather than disrupting them to obtain a desired result is a significantly different approach.

The unique combination of just at sleep acetyl-carnitine(500 mg) and low dose L-ornithine (typically 20-30 milligrams) technique is unique in that it augments rather than interrupts the normal 1.5 hours after sleep level of growth hormone release. Instead of disorganizing the normal physiological cycles, this technique augments them. This is precisely why the normal 1.5 hour measurement of growth hormone release was used to document this method. growth hormone release at any physiological cost to the organism is NOT the purpose of this technique.

Furthermore, when using this novel combination of just at sleep acetyl-carnitine(500 mg) and low dose L-ornithine (typically 20-30 milligrams) technique, a diminution of the supplemental acetyl-carnitine level to 250 mg abrogates the 1.5 hour growth hormone release level to near baseline levels as was published in the scientific literature by the author to document this new method and cited in the patent application with a copy delivered in the reference data (2) . Thus, a true synergy is apparent in that diminution of the acetyl-carnitine level abrogates the effects of these very small levels of L-ornithine (typically 20-30 milligram range). This refutes the examiners contention that the effect is due to ornithine alone. The stated goal of this patent is to augment normal physiological release, not to get growth hormone release at any cost to the normal physiological organization of the night time sleep pattern.

It is also critical to understand that the technique to augment (only) the night time growth hormone release by a just at sleep supplemental

injection of acetyl-carnitine(500 milligrams) and 20 to 30 milligrams of L-ornithine is also abrogated by any other amino acid intake due to competitive uptake problems. If the “just sufficient absorbed levels” of these two compounds are prevented by any competing amino acids (or a recent meal supplying competing amino acids) , the augmentation of normal 1.5 hour post sleep normal physiological growth hormone release is abrogated. This is the reason for the need for a minimum of a 3 hour fast prior to sleep with my technique.

RESPONSE TO #2

The citation of Giampapa (US 5895625) does not apply for several reasons. First, the separate morning, midday, and night time formulations are described as able to be taken with meals, contrary to my finding that any additional amino acid competition (such as meals or any other competing amino acids for uptake) abrogates the effect of the technique in this patent application. Second, the NIGHT TIME Growth Hormone FORMULA described in Giampapa contains acetyl-l-carnitine and many other components including protein and amino acids that interfere with the process described in this patent, but does not contain l-ornithine. Thirdly, the “MORNING DAYTIME ” components of Giampapa contains l-ornithine and acetyl-l-carnitine as well as many other amino acid components, but this says nothing about use for night time growth hormone augmentation as detailed above in

NIGHT TIME Growth Hormone Formula components of Giampapa. It is well established that day time growth hormone release (exercise and glucose/insulin sensitive) is not triggered by the same neuronal controls as the night time growth hormone release, namely, a neuronal triggered event phased to the sleep cycle state (occurring at the end of the first and second 1.5 hour night time sleep cycles). Thus, at no time does Giampapa teach that both acetyl-L-carnitine and L-ornithine acting in synergy when administered just before sleep will augment night time growth hormone release as specifically stated in my patent application. One can speculate why Giampapa intentionally or unintentionally left the L-ornithine component out of his NIGHT TIME GROWTH HORMONE FORMULA, but the reasons probably relate to the untoward stimulation and sleep disturbances of high ornithine levels documented above. My patent application surmounts this problem by the use of a novel synergy taking place with extremely low levels of L-ornithine with acetyl-carnitine that augments normal night time growth hormone release as shown by the 1.5 hours post sleep measurements. Giampapa does not understand or teach this fundamental novel understanding, nor does his NIGHT TIME GROWTH HORMONE FORMULA contain both acetyl-carnitine and L-ornithine, to say nothing of the extremely novel low levels of L-ornithine needed to in this novel synergy (or the need for an absence of competing amino acids in the mix corresponding to a minimal 3 hour fast).

Please note that the included patent by White (US 6,346,246 B1) contains a formulation that includes multiple amino acids but fails to specify both l-ornithine and acetyl-carnitine. Thus, it does not teach the need for acetyl-carnitine and ornithine just at sleep after a 3 hour fast.

REFERENCES

1. Ranke, MB. "Growth Hormone Insufficiency: Clinical Features, Diagnosis, and Therapy." [Philadelphia] 1995, Endocrinology 3 rd Ed.:
2. Parr, TB. "A New Technique to Elevate of Night Time Growth Hormone Release and a Potential Growth Hormone Feedback Control Loop." Medical Hypotheses. 56 (2001): 610-613.

TyParr